Phase-Amplitude Coupled DCM and Time-Frequency Analysis of EEG Data from AD Patients

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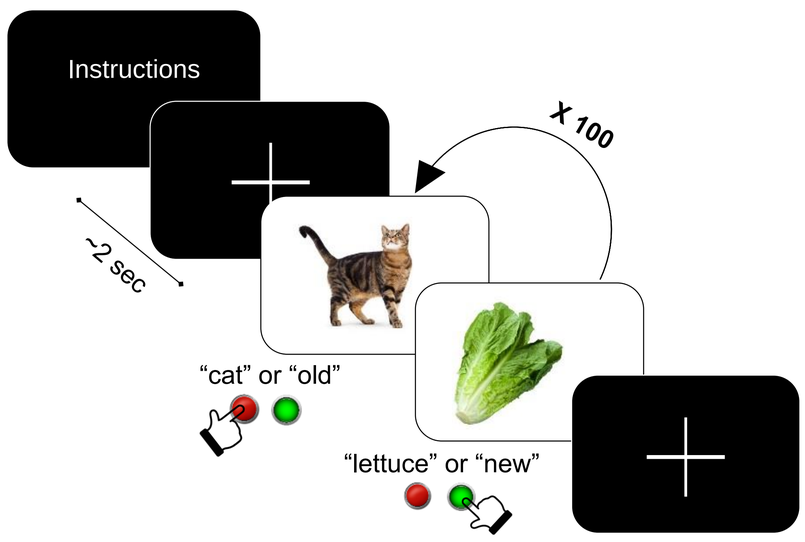
1. Abstract

We interrogated EEG time-frequency data in bilateral temporo-frontal cortical networks in AD patients, non-AD dementia patients and age-matched healthy controls. We found increased gamma activity in AD patients compared to controls, and in controls' novel trials compared to repeated trials indicating a potential prediction error. We then applied two dynamic causal models (DCMs) to test the slow amplitude envelope of signal transmission through the network, and for phase-amplitude coupling to each individuals' recordings. Slow envelope analysis revealed a loss of temporo-frontal connectivity specifically in AD patients. Phase-amp DCMs revealed strong correlations between oscillator amplitudes in bilateral top-down and bottom-up connections in AD patients, which did not appear in controls or non-AD patients.

2. Background

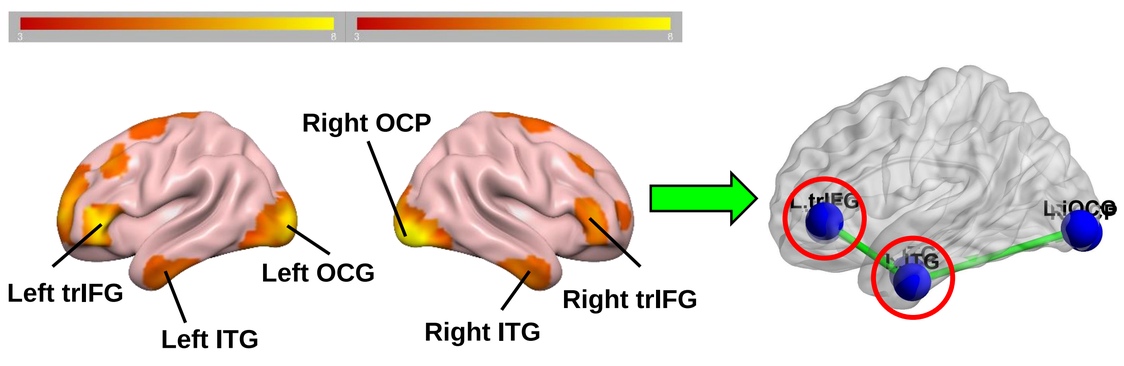
- Alzheimer's disease (AD) is the most prevalent cause of dementia in older adults, accounting for approximately two-thirds of dementia cases.
- AD initially presents with a decline in explicit (recognition) memory, and implicit (priming) memory is preserved during early stages of the disease, which begins to decline during later stages of AD[1,2].
- Medial temporal lobe atrophy is a strong indicator of developing AD in non-demented individuals, and has been implicated in explicit memory processing.
- Oscillatory power at low frequencies, including theta (4 – 8 Hz), has been found to significantly increase in scalp recordings of temporal and frontal regions during successful episodic memory recall[3].

3. Methods: Visual Memory Task



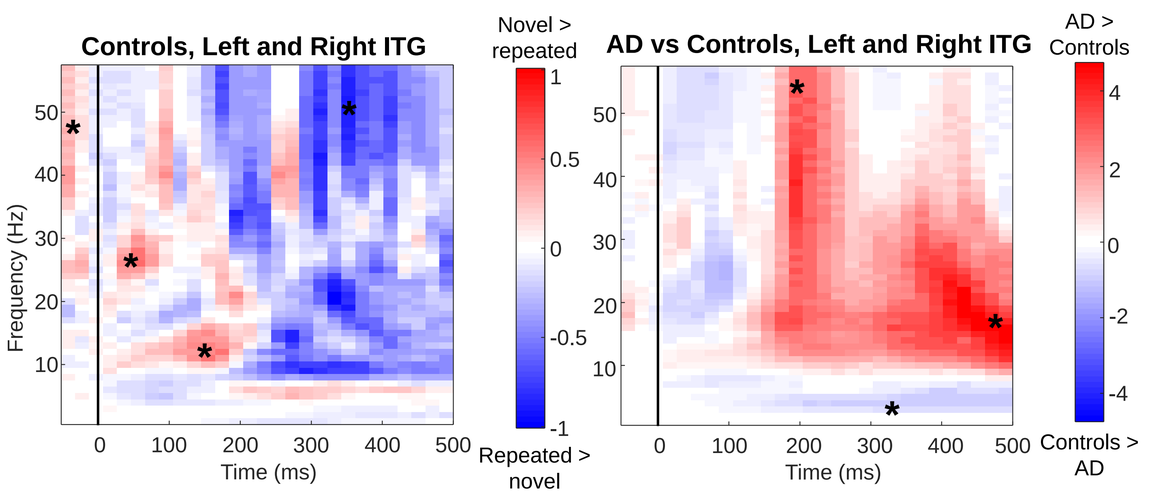
21 AD patients, 16 non-AD dementia patients (12 Vascular dementia (VD), 2 Fronto-temporal dementia (FTD), 1 alcohol-induced dementia, 1 mixed-AD/VD) and 21 healthy age-matched controls performed two behavioural memory tasks while 64-channel EEG recordings were taken. All EEG data pre-processing and analyses were conducted with SPM12.

4. 3D Source Localisation and Extraction



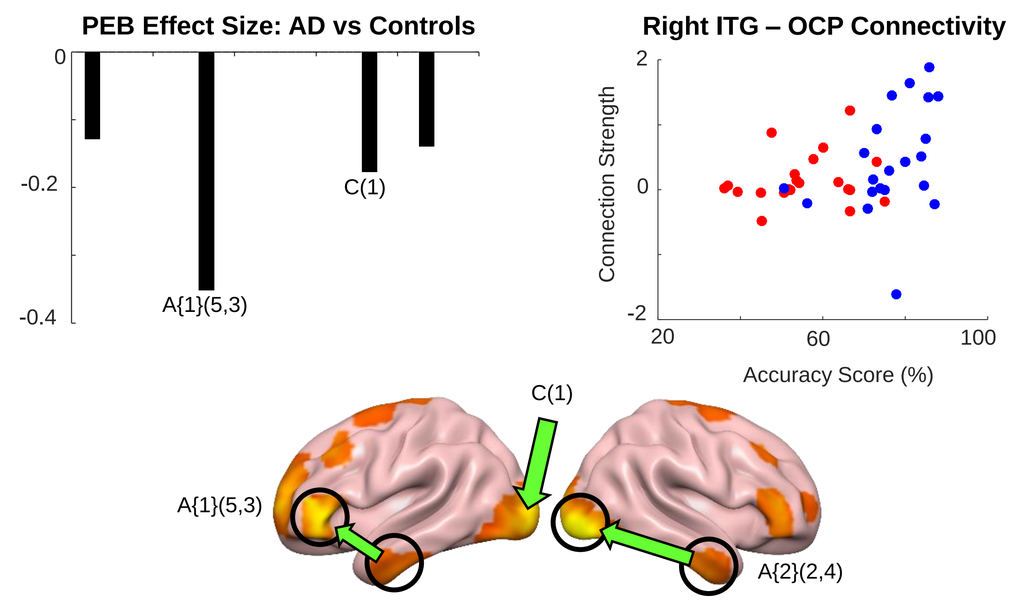
Left: One-sample t-tests identified sources of significant activity in a 3D Source Reconstruction, for all patients and controls. Six sources were identified for the recognition task: left inferior occipital gyrus (OCG), right occipital pole (OCP), left and right inferior temporal gyri (ITG), and left and right triangular part of inferior frontal gyri (IFG). Right: MNI coordinates for the left and right ITG and left and right IFG (circled in red) were used in the source extraction for time-frequency analysis. Family-wise error (FWE) corrected ($p < 0.05$).

5. Time-Frequency Analyses Show Increased Gamma Activity in AD and Novel Trials



Left: Novel trials show greater early gamma activity ($p = 0.002$, $p = 0.032$) and mid-trial beta activity ($p = 0.018$) than repeated trials in controls ITG, whereas repeated trials show greater late gamma activity than novel trials in control ITG ($p = 0.001$). Right: AD patients show greater gamma power mid-trial than controls ($p = 0.041$), and controls show greater theta activity towards the end of the trial than AD patients ($p = 0.033$), in ITG. AD patients also show significantly greater beta activity in ITG at the end of the trial compared to controls ($p = 0.011$). Black line indicates stimulus onset (time = 0 ms); asterisks indicate significant differences in power.

6. Parametric Empirical Bayes (PEB) Reveals Frontotemporal Circuit Dropout in AD



Top left: PEB effect sizes of significant parameter value differences between AD patients and controls (recognition task). Parameters: Bottom-up connections from left ITG - left IFG (A{1}(5,3)) and subcortical input into the left iOCG (C(1)). A{1}(5,3) and C(1) decreased in AD patients compared to controls. Top right: Top-down connections from right ITG - right OCP (A{2}(2,4)), shows significant positive correlation with accuracy score in AD patients and controls. Patients = red, controls = blue.

7. Conclusions

- Our results show increased gamma activity in ITG in novel compared to repeated trials, and in AD patients compared to controls which may indicate a prediction error in recognition memory tasks.
- Also, controls show increased ITG theta activity compared to AD patients, which has been linked to recall and recognition memory.
- PEB analysis of slow envelope DCMs found that left hemisphere connectivity between frontal and temporal regions are compromised in AD, suggesting explicit memory circuit dropout

8. References

[1] Golby, A. et al. (2005) 'Memory Encoding in Alzheimer's Disease: an fMRI Study of Explicit and Implicit Memory' *Brain. 128: 773-787*
[2] Wang, W. et al. (2014) 'Activity Reductions in Perirhinal Cortex Predict Conceptual Priming and Familiarity-based Recognition' *Neuropsychologia. 52: 19-26*
[3] Sederberg, P.B. et al. (2003) 'Theta and Gamma Oscillations during Encoding Predict Subsequent Recall' *The Journal of Neuroscience. 23: 10809-10814*
[4] Fagerholm, E.D. et al. (2018) 'Breaking the bonds of Weak Coupling: The Dynamic Causal Modelling of Oscillator Amplitudes' *Submitted*